Cardiac and skeletal muscle effects in the randomized HOPE-Duchenne trial.

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Public Summary:
HOPE-Duchenne is a phase I/II randomized, controlled, open-label trial designed to evaluate the safety and explore the efficacy of intracoronary CAP-1002, in patients with DMD with cardiomyopathy. Here we report the results of Halt Cardiomyopathy Progression (HOPE)–Duchenne, a clinical trial of allogeneic CDCs (CAP-1002). Cardiac function and structure were assessed by MRI. Given the preclinical observations of improved skeletal muscle function, we also investigated changes in performance of the upper limb (PUL) and other assessments of dystrophic skeletal muscle function. Unlike most clinical trials in DMD, which target younger ambulatory patients, we studied an older population with more advanced disease. HOPE participants were predominantly nonambulatory and had substantial cardiomyopathy without heart failure; they had severe limitation in shoulder function but preserved, albeit compromised, middle and distal upper limb function. Thus, in the HOPE population, both cardiac and upper limb function were optimally situated between severe loss of function, from which recovery would be extraordinary, and normal function, upon which it is impossible to improve. The concordant signals of efficacy in the HOPE-Duchenne trial in heart and skeletal muscle suggest not just slowed disease progression, but net improvements from baseline. In brief, we report that a treatment originally targeted at DMD cardiomyopathy could potentially benefit both cardiac and skeletal muscle.

Scientific Abstract:
OBJECTIVE: To assess the feasibility, safety, and efficacy of intracoronary allogeneic cardiosphere-derived cells (CAP-1002) in patients with Duchenne muscular dystrophy (DMD). METHODS: The Halt Cardiomyopathy Progression (HOPE)-Duchenne trial is a phase I/II, randomized, controlled, open-label trial (NCT02485938). Patients with DMD >12 years old, with substantial myocardial fibrosis, were randomized (1:1) to usual care (control) or global intracoronary infusion of CAP-1002 (75 million cells). Participants were enrolled at 3 US medical centers between January and August 2016 and followed for 12 months. An independent Data and Safety Monitoring Board provided safety oversight. Cardiac function and structure were assessed by MRI, and analyzed by a blinded core laboratory. Skeletal muscle function was assessed by performance of the upper limb (PUL). RESULTS: Twenty-five eligible patients (mean age 17.8 years; 68% wheelchair-dependent) were randomized to CAP-1002 (n = 13) or control (n = 12). Incidence of treatment-emergent adverse events was similar between groups. Compared to baseline, MRI at 12 months revealed significant scar size reduction and improvement in inferior wall systolic thickening in CAP-1002 but not control patients. Mid-distal PUL improved at 12 months in 8 of 9 lower functioning CAP-1002 patients, and no controls (p = 0.007). CONCLUSIONS: Intracoronary CAP-1002 in DMD appears safe and demonstrates signals of efficacy on both cardiac and upper limb function for up to 12 months. Thus, future clinical research on CAP-1002 treatment of DMD cardiac and skeletal myopathies is warranted. CLASSIFICATION OF EVIDENCE: This phase I/II study provides Class II evidence that for patients with DMD, intracoronary CAP-1002 is feasible and appears safe and potentially effective.